Escola Tècnica Superior d'Enginyeria de Telecomunicació de Barcelona

Data-driven CM to H&E transformation

by

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supervised by

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September 18, 2019

Abstract

CM... DL...

Acknowledgments

Thanks to...

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Acronyms

ANNs Artificial Neural Networks.

CM Confocal Microscopy.

DL Deep Learning.

FCM Fluorescence Confocal Microscopy.

GANs Generative Adversarial Networks.

H&E Hematoxylin and Eosin stain.

ML Machine Learning.

NN Neural Network.

RCM Reflectance Confocal Microscopy.

1 Introduction

1.1 Project Background

In recent years, Deep Learning (DL) has significantly improved the performance of a wida range of computer vision tasks like image classification, object detection or segmentation tasks. Generative Adversarial Networks (GANs) in particular have revolutionized generative tasks like image synthesis and image-to-image translation. Image-to-image translation is the problem where we have a source image and we want to generate an image based on the source but with different characteristics.

In this work, the idea of image-to-image translation is applied to the transformation of Confocal Microscopy (CM) histological images into Hematoxylin and Eosin stain (H&E) appearance.

1.1.1 Confocal microscopy

CM is an optical imaging technique for increasing optical resolution and contrast of a micrograph by means of using a spatial pinhole to block out-of-focus light in image formation. With it, technician are able to slice thin sections out of thick fluorescent specimens, view specimens in planes tilted to the line of sight, penetrate deep into light-scattering tissues, obtain 3D views at very high resolution... (Inoué 2006)

Ex vivo[1] confocal scanning laser microscopy can potentially accelerate Mohs surgery[2] by rapidly detecting carcinomas without conventional frozen histopathology. (Chung et al. 2005)

Two different CM modes exist, Reflectance Confocal Microscopy (RCM) displays the backscattering signal of naturally occurring skin components, whereas Fluorescence Confocal Microscopy (FCM) provides contrast by using an applied fluorescent dye (Skvara et al. 2012).

[1]Ex vivo means that which takes place outside an organism. In science, ex vivo refers to experimentation or measurements done in or on tissue from an organism in an external environment with minimal alteration of natural conditions.

[2]Mohs micrographic surgery is considered the most effective technique for treating many basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs), the two most common types of skin cancer. The procedure is done in stages, including lab work, while the patient waits. This allows the removal of all cancerous cells for the highest cure rate while sparing healthy tissue and leaving the smallest possible scar.

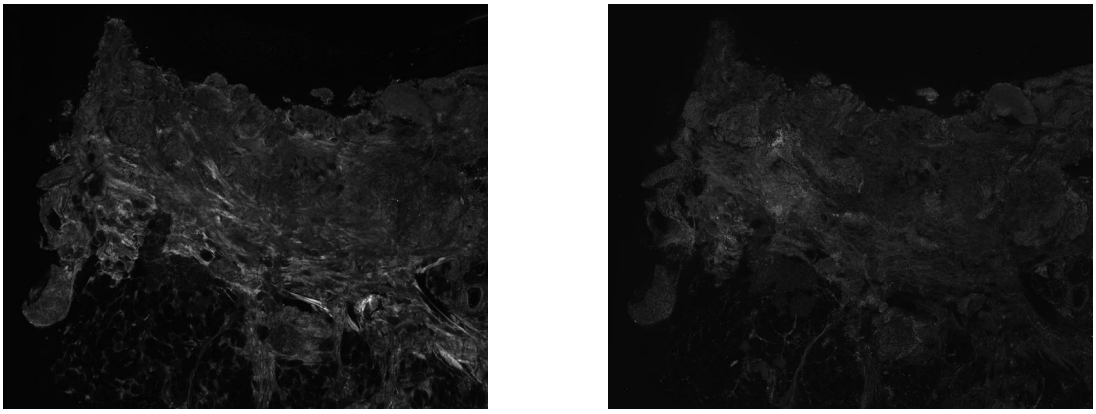


Figure 1: Example of a CM micrograph of a skin tissue. Reflectance mode on the left and fluorescence mode on the right

1.2 Problem statement

CM has enabled rapid evaluation of tissue samples directly in the surgery room significantly reducing the time of complex surgical operations in skin cancer (Cinotti et al. 2018), but the output largely differs from the standard H&E slides that pathologists typically use to analyze tissue samples.

To bridge this gap, a method for combining the aforementioned modes of CM into a H&E-like image is presented in this work. A correctly done CM to H&E mapping would bring the efficiency of CM to untrained pathologists and surgeons.

Similar to a false color (also knows as pseudo color) transformation, a parametric mapping function can be defined:

$$\mathbf{DSCM} = f_\theta(\mathbf{R}, \mathbf{F}) \tag{1}$$

where $\mathbf{DSCM} \in \mathbb{R}^{3\times H\times W}$ (stands for digitally-stained CM) represents the resulting H&E-like RGB image, $\mathbf{R} \in \mathbb{R}^{H\times W}$ and $\mathbf{F} \in \mathbb{R}^{H\times W}$ represent the reflectance and fluorescence modes (respectively) of the CM input image with height H and width W.

1.2.1 Affine transformation

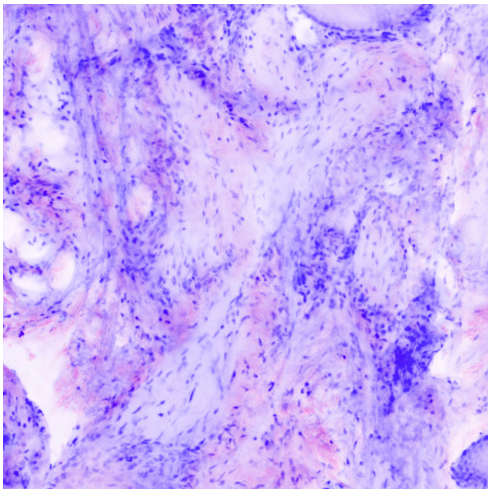
An affine transfomation is proposed in Gareau 2009 for the function f where each channel (c) is computed as:

$$\mathbf{DSCM}_{c,:} = \mathbf{1} - \mathbf{F}(1 - \mathrm{H}_c) - \mathbf{R}(1 - \mathrm{E}_c) \tag{2}$$

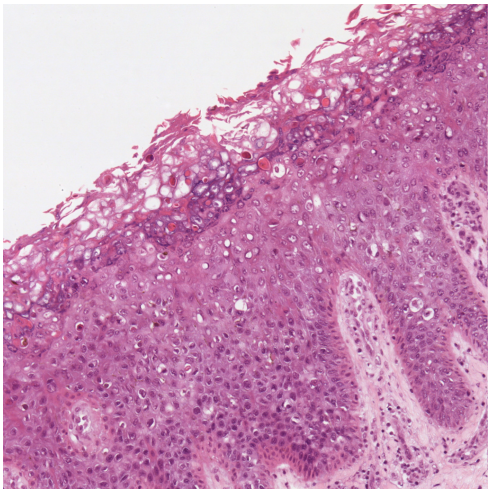
where:

$$\mathbf{H} = \begin{bmatrix} 0.30 & 0.20 & 1 \end{bmatrix}$$
$$\mathbf{E} = \begin{bmatrix} 1 & 0.55 & 0.88 \end{bmatrix}$$

These vectors represent coordinates in the RGB space (and). This way, the CM modes highlight different structures in distinct colours similar to a H&E slide; but as it can be seen in figure 2, the color scheme differs from an actual H&E sample.



(a) Digitally stained sample using the affine transformation

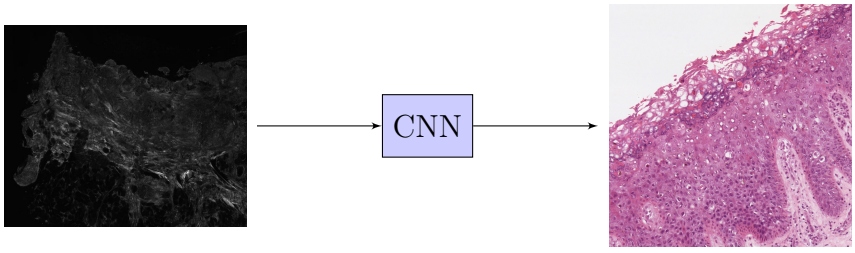


(b) H&E stained sample

Figure 2: Comparison between digital stain and H&E stain

1.2.2 Data-driven approach

In contrast to Gareau 2009 work where the parameters (**H** and **E**) are found experimentally, a data-driven approach of the problem will be taken where the parameters of the mapping function 1 are found based on data. More specifically, the transformation will be defined by a Neural Network (NN) and the parameters will be searched through an adversarial setting.



1.3 Methods and procedures

This project was carried out at the Image and Video Processing Group (GPI) research group from the Signal Theory and Communications Department (TSC) at the Universitat

Politecnica de Catalunya (UPC) in collaboration with the Dermatology Department from the Hospital Clínic de Barcelona.

The work presented in this thesis is the natural continuation of the work presented in Combalia et al. 2019...

1.4 Document Structure

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2 Theoric background

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2.1 Artificial Neural Networks

Artificial Neural Networks (ANNs) were originally developed as a mathematical model of the biological brain (McCulloch and Pitts 1943; Rosenblatt 1958; Rumelhart and McClelland 1987). Although ANNs have little resemblance to real biological neurons, they are a powerful Machine Learning (ML) tool and one of the most popular research topics in the last years. Nowadays, most researchers have shifted from the prespective of the biological neuron model to a more general *function approximator* point of view, as it was proved that ANNs with enough capacity are capable of approximating any measurable function to any desired degree of accuracy (Cybenko 1989; Hornik 1991).

2.1.1 Perceptron

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2.1.2 Multi-layer perceptron (MLP)

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2.1.3 Convolutional Neural Networks (CNN)

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Fully-convolutional Networks

2.1.4 Generative Adversarial Networks (GANs)

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GANs Proof of Concept Morbi luctus, wisi viverra faucibus pretium, nibh est placerat odio, nec commodo wisi enim eget quam. Quisque libero justo, consectetuer a, feugiat vitae, porttitor eu, libero. Suspendisse sed mauris vitae elit sollicitudin malesuada. Maecenas ultricies eros sit amet ante. Ut venenatis velit. Maecenas sed mi eget dui varius euismod. Phasellus aliquet volutpat odio. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Pellentesque sit amet pede ac sem eleifend consectetuer. Nullam elementum, urna vel imperdiet sodales, elit ipsum pharetra ligula, ac pretium ante justo a nulla. Curabitur tristique arcu eu metus. Vestibulum lectus. Proin mauris. Proin eu nunc eu urna hendrerit faucibus. Aliquam auctor, pede consequat laoreet varius, eros tellus scelerisque quam, pellentesque hendrerit ipsum dolor sed augue. Nulla nec lacus.

GANs for image-to-image translation

- Pix2Pix
- CycleGANs

3 Methodology

3.1 Despeckling network

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3.1.1 Speckle noise

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Proposed network architectures Nulla malesuada porttitor diam. Donec felis erat, congue non, volutpat at, tincidunt tristique, libero. Vivamus viverra fermentum felis. Donec nonummy pellentesque ante. Phasellus adipiscing semper elit. Proin fermentum massa ac quam. Sed diam turpis, molestie vitae, placerat a, molestie nec, leo. Maecenas lacinia. Nam ipsum ligula, eleifend at, accumsan nec, suscipit a, ipsum. Morbi blandit ligula feugiat magna. Nunc eleifend consequat lorem. Sed lacinia nulla vitae enim. Pellentesque tincidunt purus vel magna. Integer non enim. Praesent euismod nunc eu purus. Donec bibendum quam in tellus. Nullam cursus pulvinar lectus. Donec et mi. Nam vulputate metus eu enim. Vestibulum pellentesque felis eu massa.

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3.2 Stain Network

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3.2.1 Proposed architecture

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4 Experiments and results

4.1 Result validation

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4.1.1 Experiments

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4.1.2 Histology Professionals Validation

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5 Conclusions and future development

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